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| PTO/SB/08A<br><br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br>(Use as many sheets as necessary)<br><br><div style="border: 1px solid black; border-radius: 50%; width: 100px; height: 100px; display: flex; align-items: center; justify-content: center; margin: 0 auto;">             AUG 13 2003           </div> |   |                      |                        | <b>Complete if Known</b> |                    |
|  |   | Application Number   | 09/857,876             |                          |                    |
|  |   | Filing Date          | October 5, 2001        |                          |                    |
|  |   | Confirmation Number  | Unknown                |                          |                    |
|  |   | First Named Inventor | John P. McKearn et al. |                          |                    |
|  |   | Group Art Unit       | 1614                   |                          |                    |
|  |   | Examiner Name        | Unknown                |                          |                    |
| Sheet  | 1 | of                   | 4                      | Attorney Docket No.      | PHA 4292 (3167/2Z) |

**U.S. PATENT DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | U.S. Patent Document |                                      | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document<br>MM-DD-YYYY |
|--------------------|-----------------------|----------------------|--------------------------------------|---|---|
|                    |                       | Number               | Kind Code <sup>2</sup><br>(if known) |   |   |
| CM                 | 1.                    | 4,140,707            |                                      | Cleare et al.                                   | 02-20-1979  |
| ✓                  | 2.                    | 5,672,583            |                                      | Chapman et al.                                  | 09-30-1997  |
| ✓                  | 3.                    | 5,837,696            |                                      | Golub et al.                                    | 11-17-1998  |

**FOREIGN PATENT DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | Foreign Patent Document |                     |                                      | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document<br>MM-DD-YYYY | T <sup>6</sup> |
|--------------------|-----------------------|-------------------------|---------------------|--------------------------------------|---|---|----------------|
|                    |                       | Office                  | Number <sup>4</sup> | Kind Code <sup>2</sup><br>(if known) |   |   |                |
| CM                 | 4.                    | EP                      | 0 640 594           | A1                                   | Fujirebio Inc.                                  | 03-01-1995  |                |
| ✓                  | 5.                    | EP                      | 0 716 086           | A1                                   | Boehringer Mannheim GMBH                        | 06-12-1996  |                |
| ✓                  | 6.                    | EP                      | 0 758 649           | A1                                   | Kureha Chemical Industry Co., Ltd.              | 02-19-1997  |                |
| ✓                  | 7.                    | EP                      | 0 818 443           | A2                                   | American Cyanamid Company                       | 01-14-1998  |                |
| ✓                  | 8.                    | GB                      | 2 282 598           | A                                    | Merck & Co., Inc.                               | 04-12-1995  |                |
| ✓                  | 9.                    | WO                      | 93/00427            | A2                                   | Erziehungsdirektion of the Canton Zurich        | 01-07-1993  |                |

|                    |  |                 |          |
|--------------------|--|-----------------|----------|
| Examiner Signature |  | Date Considered | 12-28-03 |
|--------------------|--|-----------------|----------|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached or place an "A" here if English language abstract is attached..

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|   |                     | First Named Inventor     | John P. McKear et al. |
|   |                     | Group Art Unit           | 1614                  |
|   |                     | Examiner Name            | Unknown               |
| Sheet 2 of 4  | Attorney Docket No. | PHA 4292 (3167/2Z)       |                       |

|     |    |          |    |  |            |
|-----|----|----------|----|--|------------|
| 10. | WO | 94/02466 | A1 | The Du Pont Merck Pharmaceutical Company | 02-03-1994 |
| 11. | WO | 94/21612 | A1 | Otsuka Pharmaceutical Co., Ltd.          | 09-29-1994 |
| 12. | WO | 95/13289 | A1 | Chiroscience Limited                     | 05-18-1995 |
| 13. | WO | 95/29892 | A1 | The Du Pont Merck Pharmaceutical Company | 11-09-1995 |
| 14. | WO | 96/00214 | A1 | Ciba-Geigy AG                            | 01-04-1996 |
| 15. | WO | 96/15096 | A1 | Bayer Corporation                        | 05-23-1996 |
| 16. | WO | 96/23791 | A1 | Syntex Inc.                              | 08-08-1996 |
| 17. | WO | 96/27583 | A1 | Pfizer Inc.                              | 09-12-1996 |
| 18. | WO | 97/11693 | A1 | 3-Dimensional Pharmaceuticals, Inc.      | 04-03-1997 |
| 19. | WO | 97/19068 | A1 | Warner-Lambert Company                   | 05-29-1997 |
| 20. | WO | 97/23459 | A1 | Warner-Lambert Company                   | 07-03-1997 |
| 21. | WO | 97/36497 | A2 | Mars, Incorporated                       | 10-09-1997 |
| 22. | WO | 97/44315 | A1 | Warner-Lambert Company                   | 11-27-1997 |
| 23. | WO | 97/47599 | A1 | Fujisawa Pharmaceutical Co., Ltd.        | 12-18-1997 |
| 24. | WO | 97/48685 | A1 | Glaxo Group Limited                      | 12-24-1997 |
| 25. | WO | 98/03166 | A1 | Monsanto Company                         | 01-29-1998 |
| 26. | WO | 98/05635 | A1 | Chiroscience Limited                     | 02-12-1998 |
| 27. | WO | 98/08814 | A1 | The Procter & Gamble Company             | 03-05-1998 |
| 28. | WO | 98/08850 | A1 | The Procter & Gamble Company             | 03-05-1998 |

|                    |            |                 |          |
|--------------------|------------|-----------------|----------|
| Examiner Signature | <i>CPM</i> | Date Considered | 12-28-03 |
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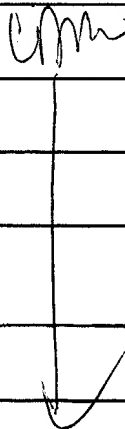
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|   |                     | Examiner Name            | Unknown                |
| Sheet 3 of 4  | Attorney Docket No. | PHA 4292 (3167/2Z)       |                        |

|     |    |          |    |                                    |            |   |
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| 30. | WO | 98/22101 | A2 | G.D. Searle & Co.                  | 05-28-1998 |   |
| 31. | WO | 98/27069 | A1 | Fujisawa Pharmaceutical Co., Ltd.  | 06-25-1998 |   |
| 32. | WO | 98/33768 | A1 | Pfizer Products, Inc.              | 08-06-1998 |   |
| 33. | WO | 98/33788 | A1 | Pharmacia & Upjohn S.P.A.          | 08-06-1998 |   |
| 34. | WO | 99/21583 | A1 | Warner-Lambert Company             | 05-06-1999 |   |

### OTHER ART - NON PATENT LITERATURE DOCUMENTS

| Examiner Initials*  | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>6</sup> |
|---|-----------------------|--|----------------|
|  | 35.                   | BROWN, F.K., et al., Matrix Metalloproteinase Inhibitors Containing a (Carboxyalkyl)amino Zinc Ligand: Modification of the P1 and P2' Residues, J. Med. Chem., 1994, pp. 674-688, Vol. 37  |                |
|   | 36.                   | CHERNEY, R.J., et al., Macrocyclic Amino Carboxylates as Selective MMP-8 Inhibitors, J. Med. Chem., 1998, pp. 1749-1751, Vol. 41   |                |
|   | 37.                   | DENIS, L.J., et al., Matrix metalloproteinase inhibitors: Present achievements and future prospects, Investigational New Drugs, 1997, pp. 175-185, Vol. 15   |                |
|   | 38.                   | GALARDY, R.E., et al., Inhibition of Angiogenesis by the Matrix Metalloprotease Inhibitor N-[2R-2-(Hydroxamidocarbonylmethyl)-4-methylpentanoyl]-L-tryptophan Methylamide, Cancer Research, Sept. 1, 1994, pp. 4715-4718, Vol. 54                              |                |
|   | 39.                   | GEARING, A.J.H., et al., Processing of tumour necrosis factor- $\alpha$ precursor by metalloproteinases, Letters to Nature, Aug. 18, 1994, pp. 555-557, Vol. 370   |                |
|   | 40.                   | International Search Report for Application No. PCT/US99/30676, dated July 18, 2000  |                |

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| Sheet 4 of 4  | Attorney Docket No. | PHA 4292 (3167/2Z)       |                        |

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| 41. | JACOBSON, I.C., et al., Structure-Based Design and Synthesis of a Series of Hydroxamic Acids with a Quaternary-Hydroxy Group in P1 as Inhibitors of Matrix Metalloproteinases, Bio-Organic & Medicinal Chemistry Letters, 1998, pp. 837-842, Vol. 8 |  |
| 42. | LARK, M.W., et al., <i>In Vivo</i> Activity of Human Recombinant Tissue Inhibitor of Metalloproteinases (TIMP), Biochem Pharmacol, 1990, pp. 2041-2049, Vol. 39, No. 12   |  |
| 43. | McGEEHAN, G.M., et al., Regulation of tumor necrosis factor- $\alpha$ processing by a metalloproteinase inhibitor, Letters to Nature, Aug. 18, 1994, pp. 558-561, Vol. 370  |  |
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| 45. | NAITO, K., et al., Inhibition of Growth of Human Tumor Cells in Nude Mice by a Metalloproteinase Inhibitor, Int. J. Cancer, 1994, pp. 730-735, Vol 58   |  |
| 46. | PRATT, L.M., et al., Bioorganic Medicinal Chemistry Letters, 1998, pp. 1359-1364, Vol. 8  |  |
| 47. | RASMUSSEN, H.S., et al., Matrix Metalloproteinase Inhibition as a Novel Anticancer Strategy: A Review with Special Focus on Batimastat and Marimastat, Pharmacol. Ther., 1997, pp. 69-75, Vol. 75, No. 1  |  |
| 48. | SOORI, G.S., et al., Phase II Study of Chemo-Biotherapy with Chlorambucil and Alpha Interferon in Patients with Non-Hodgkin's Lymphoma (NHL), Abstract #4032, Blood, 1998, pp. 240b, Vol. 92, No. 10  |  |
| 49. | THOMAS, C.A., et al., High-Dose Methotrexate (HD-MTX) Monotherapy in Patients with CNS Non-Hodgkin's Lymphoma, Blood, 1998, Abstract #4033, pp. 240b, Vol. 92, No. 10   |  |
| 50. | VON ROEDERN, E.G., et al., Design and Synthesis of Malonic Acid-Based Inhibitors of Human Neutrophil Collagenase (MMP8), J. Med. Chem., 1998, pp. 339-345, Vol. 41  |  |
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| 52. | YEH, L.-A., et al., Inhibition of Metalloproteinase by Futoenone Derivatives, Bio-Organic & Medicinal Chemistry Letters, 1995, pp. 1637-1642, Vol. 5, No. 15  |  |

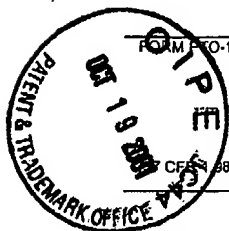
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Form PTO-1449 (Modified)



FORM FCO-1449

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

ATTY. DOCKET NO.

**CU-2557**

SERIAL NO.

09/857,876

**APPLICANT**

John P. McKearn et al

FILING DATE

**June 12, 2001**

**GROUP**

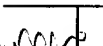
## U.S. PATENT DOCUMENTS

[illegible]

**FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION**

[illegible]

**OTHER DOCUMENTS** (Including Author, Title, Date, Place of publication)

|   |   |
|---|---|
|  | Miller, A.R. et al: "Neoadjuvant chemoradiation for adenocarcinoma of the pancreas" Surgical Oncology Clinics of North America (1998) |
|   | Takahashi, Y. "Clinical trials and strategy for anti-metastatic drugs" Biotherapy (1999)  |
| EXAMINER  | DATE CONSIDERED   |

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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